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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
09/013,871	01/27/98	MARTIN U	BOER-1059.1-

EXAMINER
GAMBEL, P

HM22/0804

FELFE AND LYNCH
805 THIRD AVENUE
NEW YORK NY 10022

ART UNIT	PAPER NUMBER
1644	8

DATE MAILED: 08/04/99

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 5/21/99

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1-28 is/are pending in the application.
Of the above, claim(s) 3, 4, 12, 25-26 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 1, 2, 5-11, 13-24, 27, 28 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☑ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 NO 119 PRIORITY CLAIMED; JEF OATH

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892
☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____ SEE OFFICE ACTION (#3)
☐ Interview Summary, PTO-413
☑ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

SEE OFFICE ACTION ON THE FOLLOWING PAGES

DETAILED ACTION

1. Applicant's election with traverse of the species L-selectin in Paper No. 7 is acknowledged. The traversal is on the ground(s) that the reasoning is hard to understand, given that there is no patentable distinction between the antibodies. This is not found persuasive because of the reasons of record set forth in Paper No. 6. This application contains claims directed to the following patentably distinct species of the claimed Invention: wherein the antibody specificity is: E-selectin, L-selectin or P-selectin. These antibody specificities are distinct because their structures and modes of action are different.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1, 2, 5-11, 13-24 and 27-28 are under consideration as they read on the elected species.

Claims 3, 4, 12, 25-26 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected species.

2. The filing date of the claims 22-28 with respect to "reducing the probability of incidence of organ failure after a polytraumatic event" as well as the non-elected targeted species of "P-selectin" and "E-selectin" are deemed to be the filing date of priority application PCT/US96/13152; as priority application USSN 08/578,953 does not provide sufficient written description for these "limitations". If applicant desires priority prior to 12/27/97 for these "limitations"; applicant is invited to point out and provide documentary support for the priority of the instant claims. Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

3. In the interest of compact prosecution and applicant's convenience the 1449's and 892's of priority application USSN 08/578,953 have been copied and placed into the instant application. The copies of the references will not be sent to applicant, since these references are already of record.

4. Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84. Please see the enclosed form PTO-948.

5. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Applicant is required to identify the nucleotide and amino acid sequences in the specification with SEQ. ID NOS.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required.

6. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 C.F.R. § 1.75(d)(1) and M.P.E.P. § 608.01(l). Correction of the following is required: It is not readily apparent where the recitation of "reducing the probability of incidence of organ failure after a polytraumatic event" is disclosed in the specification as filed.

Applicant is requested to identify the written support for this "limitation" encompassed by claims 22-28 in the specification as filed.

If no such written support is provided in the specification as filed, then applicant should amend the specification accordingly.

7. Claims 7, 8, 21-24, 27-28 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 7, 8, 21, 27 are indefinite in the recitation of "Dreg 55 or HuDreg 55, HuDreg 200" because their characteristics are not known. The use of "these terms" as the sole means of identifying the claimed antibodies renders the claim indefinite because "these terms" are merely laboratory designations which do not clearly define the claimed product, since different laboratories may use the same laboratory designations to define completely distinct cell lines or hybridomas. Applicant should amend the claims to include the SEQ ID NOS. to clearly identify the biological species.

B) Claims 22-24, 27-28 are indefinite in the recitation of "reducing the probability of incidence of organ failure after a polytraumatic event" since "reducing the probability" is a relative phrase which renders the claims indefinite. The phrase is not defined by the claim, the specification does not appear to provide a standard for ascertaining the requisite degree or statistical analysis as well as appropriate probability, and one of ordinary skill in the art would not be reasonably apprised of the scope or metes and bounds of the invention

C) The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

9. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

10. Claims 1, 2, 5-11, 13-24 and 27-28 are rejected under 35 U.S.C. § 102(b) as being anticipated by Co (WO 94/12215). Co teaches the use of humanized DREG 55 and DREG 200 antibodies to inhibit disorders or conditions encompassed by the claimed methods (e.g. ischemic events, cardiac surgery, angioplasty, multiple organ failure) and dosages which depend on the patient and therapeutic endpoint (see entire document, particularly Methods of Use). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced methods with L-selectin-specific antibodies.

11. Claims 1, 2, 5-11, 13-24 and 27-28 are rejected under 35 U.S.C. § 102(b) as being anticipated by Lefer (WO 95/95181) teaches the use of humanized DREG 200 to inhibit a number of disorders or conditions encompassed by the claimed methods (e.g. ischemic events, cardiac surgery, angioplasty, multiple organ failure) and dosages which depend on the patient and therapeutic endpoint (see entire document, particularly Therapeutic Methods). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced methods with L-selectin-specific antibodies.

12. Claims 1, 2, 6, 10, 11, 20, 22-23 and 28 are rejected under 35 U.S.C. § 102(e) as being anticipated by Tedder et al. (U.S. Patent No. 5,679,346). Tedder et al. Teaches the use of LAM-1-specific antibodies including recombinant antibodies thereof to inhibit a number of disorders or conditions encompassed by the claimed methods (e.g. neutrophil-mediated inflammation, reperfusion injury and multi-organ failure) (see entire document, including columns 6-7, overlapping paragraph). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced methods with LAM-1-specific antibodies. The LAM-1 specificity is the same as the L-selectin specificity.

13. Claims 1, 2, 5-11, 13-24 and 27-28 are rejected under 35 U.S.C. § 103 as being unpatentable over Co (WO 94/12215) AND/OR Lefer (WO 95/1515181) AND/OR Tedder et al. (U.S. Patent No.5,679,346 5,679) AND/OR Buerke et al. (J. Pharmacology and Experimental Therapeutics 271: 134-142, 1994) in view of Butcher et al. (U.S. Patent No. 5,316,913), Springer et al. (U.S. Patent No. 5,460,945), Moat et al. Ann. Thorac. Surg., 1993; 1449), Finn et al. (Perfusion, 1993). The instant claims are drawn to using L-selectin-specific antibodies in the treatment of polytraumatic events and extracorporeal circulation.

Co teaches the use of humanized DREG 55 and DREG 200 antibodies to inhibit inflammatory disorders including the conditions encompassed by the claimed methods and dosages which depend on the patient and therapeutic endpoint (see entire document, particularly Methods of Use).

Lefer teaches the use of humanized DREG 200 to inhibit a number of disorders associated with reperfusion-ischemia including the conditions encompassed by the claimed methods and dosages which depend on the patient and therapeutic endpoint (see entire document, particularly Therapeutic Methods).

Buerke et al. (J. Pharmacology and Experimental Therapeutics, 1994) Buerke et al. teach the use of humanized DREG 200 to protect from myocardial reperfusion injury and the importance of blocking neutrophil-endothelial interactions and protecting cardiac function against necrotic tissue injury (see entire document). Buerke et al. also acknowledges that this protection may occur by inhibition of neutrophil rolling along the endothelium, thereby inhibiting subsequent tight neutrophil adhesion and release of mediators with their known exacerbation (see Discussion, particularly page 141, column 1, paragraph 2). Therefore, there was expectation of success of L-selectin inhibitors in view of neutrophils shedding L-selectin upon activation. Buerke et al. differs from the instant methods by not disclosing extracorporeal circulation and polytraumatic event per se, however in treating the reperfusion injury targeted by Buerke, it would have been obvious to treat similar conditions associated with extracorporeal circulation and traumatic events that would benefit from the inhibition of neutrophil-endothelial interactions.

Tedder et al. teach the use of L-selectin-specific antibodies in the amelioration of inflammatory conditions including those encompassed by the claimed methods (see entire document, including Methods of Use and Use). These references differ from the instant methods by not disclosing the DREG 55 and DREG 200 specificity per se.

Butcher et al. teaches neutrophil L-selectin as a indicator of neutrophil activation and that DREG 55 and DREG200 were known in the prior art (see entire document, including column 5, lines 21-24).

Springer et al. teaches the use of inhibitors of neutrophil-endothelial interactions such as L-selectin antagonists (column 13, lines 42-57) including targeting the therapeutic endpoints encompassed by the instant methods (see entire document, including column 30 Section 5.11).

Moat et al. and Finn et al. teach the role of neutrophil adhesion and activation in cardiopulmonary bypass and the importance of blocking said function. As Buerke et al. points out; L-selectin-mediated inhibition confers protection in reperfusion injuries and this may occur via inhibition of neutrophil rolling along the endothelium, thereby inhibiting subsequent tight neutrophil adhesion and release of mediators with their known exacerbation.

Co, Lefer, Buerke et al. and Tedder et al. differ from the instant claimed methods by not disclosing all of the time points for administering the inhibitory L-selectin antibodies, however dosages and administration would rely upon the needs of the patient and the nature of the intended therapeutic endpoint. Co and Lefer do teach single and multiple administrations sufficient to cure or at least partially arrest the disease and its complications; which would depend on the severity of the disease and general state of the of the immune system in a patient; which can be administered as bolus or repeated injections to achieve optimal plasma levels of antibody and alone or in combination with other therapeutic agents or drugs (see Methods of Use). Also, the ordinary artisan would have expected to reduce the probability of organ failure after a polytraumatic event, given the teachings of the prior art, including Methods of Use, as taught by Co and Lefer.

Therefore, the prior art made and used L-selectin antibodies including the DREG 55 and DREG 200 specificities to inhibit inflammation including those associated with neutrophil adhesion and activation and the nature of the injuries claimed in the instant methods. The particular humanized L-selectin antibodies were known in the prior art or could have been made by routine technology at the time the invention was made. Although some of the references are silent about the exact sequences of the L-selectin-specific antibodies, the standard recombinant techniques and computer analyses of CDR known in the prior art would have resulted in the same or very nearly the same structural and functional characteristics of the instant claims since both the references and instant invention use the same techniques, the same antibody specificities and the same goals. For example, see the humanization of antibodies taught by Co and Lefer. Also, such humanization of antibodies for therapeutic uses was well known and practiced at the time the invention was made. The claimed functional limitations encompassed by the claims would be expected properties of selecting for L-selectin-specific antibodies to specifically bind and inhibit L-selectin. The claims drawn to specifically defined humanized antibodies are obvious since the record does not contain any evidence that the antibodies differ in any significant manner that one of ordinary skill in the art would expect to generate using L-selectin as the starting antigen in the basic method of generating antibodies and humanizing said antibodies. There appears no evidence that the use of various sources of framework amino acids would differ in an unexpected or distinct manner from those available to the ordinary artisan at the time the invention was made. Also, Co and Lefer appear to teach the same DREG 55/DREG 200 antibodies of the claimed invention.

One of ordinary skill in the art at the time the invention was made would have been motivated to select and evaluate the efficacy of L-selectin-specific antibodies as a therapeutic regimen in treating cardiovascular and traumatic diseases. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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July 29, 1999

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